IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application No.	:	10/564,674	Confirmation No.	:	1707
Applicants	:	MARCEL WIJLAARS et al.			
Filed	:	7/15/2004			
Title	:	TISSUE SUBSTITUTE MATERIAL			
Group Art Unit	:	1615			
Examiner	:	Caralynne Helm			
Customer No.	:	28289			

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Commissioner for Patents
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APPEAL BRIEF

Sir:

This Appeal Brief is submitted in support of the Notice of Appeal filed electronically on June 29, 2010 and received by the Patent Office on June 29, 2010. In accordance with 37 C.F.R. § 41.37, Appellants now submit this Appeal Brief, and hereby request that the rejections asserted in the Office Action be reversed, and that all pending claims be found patentable over the prior art and in condition for allowance.

I hereby certify that this correspondence is being electronically submitted to the United States Patent and Trademark Office on October 11, 2010.

10/11/2010 Mary Ann Mulvihill
Date Signature

Mary Ann Mulvihill
Typed Name of Person Signing Certificate

Table of Contents

REAL PARTY IN INTEREST

Stitching voor de Technishe Wetenschappen, the Assignee of the entire right, title, and interest to the above-identified application, is the real party in interest in this Appeal.

RELATED APPEALS AND INTERFERENCES

There are no appeals or interferences known to the Appellant, the Appellant's legal representative, or the Assignee of the above-identified application which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

STATUS OF CLAIMS

Claims 1-7 have been previously cancelled. Claims 8-15 are pending in the present application, stand finally rejected under 35 U.S.C. §103(a), and are subject to this appeal.

STATUS OF AMENDMENTS

There are no unentered amendments to the claims of this application. A copy of the claims involved in this Appeal in their current form is contained in the Claims Appendix attached hereto.

SUMMARY OF CLAIMED SUBJECT MATTER

The above-captioned application contains two pending independent claims, claims 8 and 15. A summary of claims 8 and 15 is provided below. Applicants do not separately argue that any dependent claim is patentable for any reason independent of the reasons that claims 8 or 15 is patentable. Accordingly, Applicants do not provide a summary for any dependent claim.

Claim 8 is directed to a material for cartilage-like material substitution, comprising a fibre-reinforced polymerized hydrogel.[1] The polymerized hydrogel contains 10-70% (m/m) swellable fibres (based on the dry matter).[2] The length of the fibres is at least a millimeter.[3] Additionally, 1-5% (m/m) (based on the dry matter) of a substance that contains ionized groups has been added to said polymerized hydrogel.[4] The swellable fibres have sucked up at least one monomer solution prior to polymerization of the hydrogel.[5]

Claim 15 is directed to a material for cartilage-like material substitution, comprising a fibre-reinforced polymerized hydrogel.[6] The polymerized hydrogel contains 10-70% (m/m) swellable fibres (based on the dry matter).[7] The length of the fibres is at least a millimeter.[8] One to five percent (m/m) (based on the dry matter) of a substance that contains

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[1] U.S. Publ. Pat. App. No. 2007/0173951 at ¶¶ [0004], [0008], [0009] and [0011].

[2] U.S. Publ. Pat. App. No. 2007/0173951 at ¶¶ [0004], [0006], [0007] and [0012].

[3] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0005].

[4] U.S. Publ. Pat. App. No. 2007/0173951 at ¶¶ [0004] – [0005].

[5] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0013].

[6] U.S. Publ. Pat. App. No. 2007/0173951 at ¶¶ [0004], [0008], [0009] and [0011].

[7] U.S. Publ. Pat. App. No. 2007/0173951 at ¶¶ [0004], [0006], [0007] and [0012].

[8] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0005].

ionized groups was added to said polymerized hydrogel.[9] The swellable fibres comprise at least one monomer solution.[10]

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Applicants respectfully request that the following rejections be reviewed on appeal and reversed:

1. Claims 8-9 and 12-15 stand rejected as obvious under 35 U.S.C. §103(a) over Malmonge[11] in view of Slivka[12], Pissis[13] and Young[14].

2. Claims 8 and 10-11 stand rejected as obvious under 35 U.S.C. §103(a) over Malmonge in view of Slivka, Pissis and Young as applied to claims 8-9 and 12-15 above, and further in view of Kou[15].

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[9] U.S. Publ. Pat. App. No. 2007/0173951 at ¶¶ [0004] – [0005].

[10] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0013].

[11] Malmonge *et al.*, "Artificial Articular Cartilage: Mechanoelectrical Transduction under Dynamic Compressive Loading," ARTIFICIAL ORGANS (2000) 24(3): 174-178 ("Malmonge").

[12] Slivka *et al.*, "Porous, resorbable, fiber-reinforced scaffolds tailored for articular cartilage repair," TISSUE ENGINEERING (2001) 7(6): 767-780 ("Slivka").

[13] Pissis *et al.*, "Poly(hydroxyethyl acrylate) – Nylon 6 nanocomposites. Dielectric and water sorption properties," 10TH INT'L SYMP. ON ELECTRETS (1999): 561-564.

[14] Young *et al.*, "High-strength, ultra-thin and fiber-reinforced pHEMA articial skin," Biomaterials (1998) 19: 1745-1752 ("Young").

[15] Kou *et al.*, "Modeling drug release from dynamically swelling poly(hydroxyethyl methacrylate-co-methacrylic acid) hydrogels," J. CONTROLLED RELEASE (1990) 12: 241-250 ("Kou").

ARGUMENT

Prior art replacement cartilage-like tissue had weak swelling behavior and inadequate strength and toughness.[16] This is particularly important in respect to the ability of cartilage-like tissue to swell when the composition of the fluid (water/salt) surrounding the tissue changes.[17] The invention addresses this problem by using a cartilage-like tissue containing 10-70% (m/m) swellable fibres. The length of the fibres is at least a millimeter. An example of a swellable fibre is one that contains polyurethane material.[18] The material also contains 1-5% (m/m) of a substance that contains ionized groups that is added to the polymerized hydrogel. The ionised groups provide a Donnan osmotic pressure in the hydrogel that pretensions the fibres.[19] The substance that contains ionised groups is important in maintaining the swelling ability of the material.[20]

Initially, the Examiner rejected the claims as obvious over Malmonge, Pissis and Young (and optionally in further view of Kou).[21] After only considering the Huyghe's Declaration, the Examiner saw the error in her rejection and correctly withdrew it, only to assert a new rejection based on the same references with the addition of Slivka. Thus, claim 8 stands rejected as obvious over Malmonge, Pissis Young and Slivka; and claim 15 stands rejected as

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[16] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0002].

[17] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0002].

[18] See U.S. Publ. Pat. App. No. 2007/0173951 at claim 13.

[19] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0005].

[20] U.S. Publ. Pat. App. No. 2007/0173951 at ¶ [0005].

obvious over these references in further view of Kou. However, Slivka fails to overcome or address the problems of the earlier rejection.

I. Differences between the cited references and the recited invention.

Malmonge is directed to a copolymer of HEMA and acrylic acid (AA) as artificial cartilage material.[22] The acrylic acid ionizes into acrylate and Na^+, resulting in swelling of the HEMA-AA copolymer and improvement of the compressive strength of the cartilage material.[23] The presence of ionized groups in the hydrogel at a concentration of 1.8 and 3.6% (m/m).[24] However, unlike the present invention, Malmonge does not teach the presence of relatively large fibers in the polymer gel that provide adequate strength and increased mechanical properties as required by the claimed invention.[25] Nor does Malmonge teach the incorporation of fibers into a hydrogel (which the Examiner has acknowledged).[26] Instead, Malmonge is solely concerned with the mechano-electric transaction of the HEMA-AA copolymer and its dependence on acrylic acid content.[27] Nowhere does Malmonge address providing mechanical strength and

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[21] Office Action dated December 8, 2008.

[22] Huyghe Declaration at ¶ 5.

[23] Huyghe Declaration at ¶ 5.

[24] Office Action at pages 3-4.

[25] Huyghe Declaration at ¶ 9.

[26] Office Action at page 4.

[27] Huyghes Declaration at ¶ 5.

toughness to a hydrogel, the incorporation of a fiber into a hydrogel,[28] the length of the fiber,[29] the use of 10-70% (m/m) of the fiber,[30] or the uptake of a monomer.[31]

These deficiencies were not cured by Pissis, Young or Kou. Pissis is directed toward the dielectric and water sorption properties of poly(hydroxyethyl acrylate) (pHEA) gel reinforced with Nylon nanoparticles.[32] There is no teaching or suggestion in Pissis of the use of fibers having lengths of a millimeter or greater because this reference never contemplates improving the strength or durability of the gel.[33] In fact, Pissis only teaches using Nylon in nanoparticles form,[34] which is far smaller than the recited fibers. Additionally, Pissis teaches that "the maximum weight percentage of nanoparticles in the hydrogel that could be thus obtained was 10%."[35] Thus, without regard to the required motivation to combine the references, the combination of Malmonge and Pissis does not teach the incorporation of a fiber into a hydrogel (because Pissis teaches using a nanoparticle rather than a fiber), the recited length of the fiber, the use of 10-70% (m/m) of the fiber, or the uptake of a monomer.[36] Nor does Pissis

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[28] Acknowledged by the Examiner at page 4 of the Office Action.

[29] Acknowledged by the Examiner at page 4 of the Office Action.

[30] Acknowledged by the Examiner at page 4 of the Office Action.

[31] Huyghes Declaration at ¶ 5.

[32] Pissis at Title and at page 561, § 1; Huyghe Declaration at ¶ 6.

[33] Huyghe Declaration at ¶ 6.

[34] Pissis at page 561, § 2.1.

[35] Pissis at page 561, § 2.1.

[36] Huyghes Declaration at ¶ 6.

teach that incorporating Nylon nanoparticles provides mechanical strength and toughness to a hydrogel.[37]

Young discloses an artificial skin substitute for wound dressing characterized as ultrathin (0.23nm) and containing very small amounts of fiber (less than 1.66 wt%).[38] Young solely discloses smooth, essentially two-dimensional ultrathin woven or knitted hydrogels, for which elastic strain rather than compressive strength is a prerequisite.[39] Thus, again without regard to the requisite motivation to combine, if Young was combined with Malmonge and Pissis, the combination still would not teach the use of 10-70% (m/m) of the fiber or the uptake of a monomer.

The Examiner agreed that the recited invention was not obvious over Malmonge in view of Pissis and Young or Kou, and accordingly withdrew this rejection only to contend that by further considering Slivka, the invention is obvious, even though Slivka does not overcome the deficiencies of these references. Slivka describes porous 75:25 poly(d,l-lactide-co-glycolide) scaffolds reinforced with polyglycolide fibers for articular cartilage repair using biodegradable materials.[40] Slivka's scaffold may be a gel-like matrix,[41] but certainly it is not a hydrogel as

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[37] Huyghes Declaration at ¶ 6.

[38] Huyghe Declaration at ¶ 7.

[39] Huyghe Declaration at ¶ 9.

[40] Slivka at pages 767 and 770.

[41] Office Action at page 4; Slivka at page 770.

recited in claims 8 and 15.[42] As such, this reference is not concerned with the swellability properties in water/salt surroundings and the load-bearing capacity of a swollen hydrogel. In fact, Slivka is only concerned with a biodegradable scaffold for natural cartilage build-up.[43] At best, Slivka only teaches using 2.5 mm polyglycolide fibers. Thus, without regard to the required motivation to combine the references, if Slivka is combined with Malmonge, Pissis and Young, the combination still fails to teach 10-70% (m/m) of the fiber or the uptake of a monomer.

(The Examiner only cites Kou for the proposition that it teaches using methyl acrylic acid.[44] For the purposes of this appeal, Applicants do not argue against the use of Kou for this purpose or the combination of Kou with Malmonge.)

II. The cited references fail to teach each and every limitation recited in the claims.

Every obviousness analysis begins with comparing and contrasting the references, as a whole, to the claimed subject matter.. See *Ex parte Hellums*, App. No. 09/103,704, Appeal No. 2001-2694, 2003 WL 25281923 at *4 (BPAI Jul. 15, 2003); *Ex parte Likins*, App. No. 10/010,392, Appeal No. 2004-0760, 2004 WL 4981756 at *3 (BPAI Apr. 8, 2004). Here, even assuming that the references are properly combinable and that there is a motivation to combine them (which they are not for the reasons discussed below), the references fail to teach using 10-

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[42] See Slivka at page 770.

[43] Slivka at page 768.

[44] Office Action at pages 7-8.

70% (m/m) of a fiber or the uptake of a monomer. At best, the references teach using less than 10% of a fiber.

The Examiner even acknowledges that the references "are silent in regard to the spandex fibers 'sucking up' monomer solution."[45] Yet, the Examiner contends that Young and Pissis teach preparing hydrogels with monomer solutions, and therefore, teach monomer uptake.[46] However, this reasoning is not in line with the Pissis reference.

Pissis teaches that the swelling is due to water sorption confined to the PHEA hydrogel phase, which does not contain the Nylon nanoparticles. Pissis's hydrogel is prepared by polymerizing a watery suspension of Nylon nanoparticles in a mixture containing monomers, crosslinkers and initators.[47] Consequently, the nanoparticles are not soaked in a monomer solution, and therefore, they do not "suck up" the monomer solution.[48]

Similarly, Young provides no teaching or suggestion of soaking hydrogels reinforced with fiber in a monomer solution. Instead, Young teaches that "[f]or manufacturing the composites of fiber-reinforced pHEMA membranes, three types of commercial fabrics containing nylon and elastic fibers (S), gauze (G) and low lint wipers (G) were added into the membranes as reinforcing networks."[49] Thus, Young teaches incorporating the fibers after the

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[45] Office Action at page 6.

[46] Office Action at pages 6-7.

[47] Huyghes Declaration at ¶ 13.

[48] Huyghes Declaration at ¶¶ 6 and 13.

[49] Young at page 1746.

pHEMA membrane was polymerized, and therefore, does not teach or suggest soaking the reinforced membrane in a monomer solution.

Thus, even if the references were combinable, they fail to teach a material comprising 10-70% (m/m) of a swellable fiber wherein the swellable fiber has sucked up at least one monomer solution prior to polymerization of the hydrogel. For this reason alone, the references of claims 8 and 15 (and their dependent claims) should be reversed. However, the asserted rejections also lack the required motivation or reason to combine the references.

III. <u>There is no reason or motivation to combine the references.</u>

Specifically, the Examiner has not provided any reason or motivation to incorporate Pissis's fibers at Slivka's polyglycolide fibers' lengths into Malmonge's hydrogel, or use more than 10% of Pissis's Nylon nanoparticles. When making a rejection under 35 U.S.C. §103, the Examiner has the burden of establishing a *prima facie* case of obviousness and must establish some reason to combine the references. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 131 (2007); *Takeda Chemical Industries, Ltd. v. Alpharpharm Pty., Ltd.*, 492 F.3d 1350, 1356-1357 (Fed. Cir. 2007). Here, the Examiner mistakenly believes that she can pick-over Pissis's and Slivka's teachings without explanation why one would consider disregarding the remainder of the reference.

A. There is no reason to use Nylon particles that are larger than nanometers in size.

By picks-over the teachings of Pissis, the Examiner has failed to consider Pissis, as well as the other references, as a whole. Pissis teaches reinforcing a PHEA network with a dispersion of Nylon particles in a scale of nanometers,[50] not millimeters as recited in claim 8. Thus, upon considering Pissis, one would, at best, modify Malmonge to include nanometers of Nylon particles, not millimeters.

Yet, the Examiner mysteriously concludes that millimeters of Nylon particles will likewise improve mechanical properties because Slivka teaches using 2.5 mm of polyglycolide fibers. However, there is no motivation or reason to believe that the length of polyglycolide fibers somehow suggests that longer Nylon particles will also improve mechanical properties. The two materials are different. Nylon is a synthetic polymer otherwise known as polyamide. A polyamide is not a polyglycolide. The Examiner has provided no reason why one would ever consider longer polyamides when the references only teach polyamides at nanometer lengths and polyglycolides at millimeter lengths. Nor has the Examiner provided any reason to ignore Pissis' teaching for using nanoparticles and instead use fibers.

Moreover, such a reason did not exist prior to the disclosure of the invention recited in the above-captioned application. Thus, the invention cannot be obvious.

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[50] Pissis at page 562, § 1.

B. There is no reason to use more than 10% Nylon in a hydrogel.

Pissis also teaches that "the maximum weight percentage of nanoparticles in the hydrogel that could be thus obtained was 10%; above this value the nanoparticles tend to agglomerate and their water suspension resulted in a gel-like paste which makes it unsuitable for mixing with the monomer mixture."[51] Even though Pissis teaches using less than 10%, the Examiner, nevertheless, contends that it would be obvious to use 10, 15 and 20% Nylon fibers because Slivka teaches using 5, 10, 15 and 20% polyglycolide fibers. Not only is there no explanation why one would ever expect polyamides to be a suitable substitute for polyglycolides, there is also no explanation why one would disregard Pissis's teaching of not exceeding 10% Nylon in a hydrogel. Simply because Slivka teaches using 10, 15 and 20% polyglycolides does not provide the required reason or motivation to disregard Pissis's warning against using such concentrations of Nylon.

This lack of explanation is compounded by the fact that Young also teaches using less than 10% fibers. The Examiner contends that Young teaches a fiber reinforced polyHEMA as a biomaterial.[52] The smooth artificial skin substitute materials according to Young is ultrathin (<0.23MM) and contains less than 1.66% of fiber.[53] There is no reason provided in the Office Action to disregard Young's and Pissis's teachings regarding the amount of fiber in the material. This is not surprising since such an explanation did not exist before the disclosure of the

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[51] Pissis at page 561, § 2.1.

[52] Office Action at page 5.

[53] Huyghe Declaration at ¶ 7.

invention recited in the above-captioned application. Without such an explanation, the invention cannot be obvious.

IV. The references teach away from the recited invention.

This failure to provide the required motivation to combine the references is understood because to do so would cause the Examiner to tackle another problem: that the references teach away from the recited invention. A combination of known elements will not yield predictable results if the references teach away from the claimed invention. *Takeda Chemical*, 492 F.3d at 1359; *Ortho-McNeil Pharmaceutical, Inc. v. Mylan*, 520 F.3d 1358, 1364 (Fed. Cir. 2008); and *Ex parte Ikeda*, App. No. 08/352,079, Appeal No. 2008-0492, Slip Op. at 7 (BPAI Mar. 26, 2008).

A. The cited references teach a material containing less than 10% fiber.

Both Young and Pissis teach a material containing less than 10% fiber. Pissis teaches that the maximum weight percentage of nanoparticles in the hydrogel that could be obtained by Pissis was 10% before undesired agglomeration occurs resulting in a gel-like paste which makes the hydrogel unsuitable for mixing with a monomer mixture.[54] Therefore, Pisses teaches away from using 10-70% (m/m) swellable fibres.

[54] Pissis at page 561, § 2.1.

Likewise, Young teaches that the smooth artificial skin substitute materials gis ultrathin (<0.23MM) and contains less than 1.66% of fiber.[55] Thus, Young also teaches away from using 10-70% (m/m) swellable fibres.

B. Pissis teaches using fibers having a length less than one millimeter.

Furthermore, as discussed above, Pissis teaches using Nylon having a length in the order of nanometers, not millimeters. In fact, Pissis teaches taking larger Nylon fibers and purposefully reducing the fibers' size to nanoparticles.[56]

V. The Huyghe Declaration provides unexpected results.

On June 8, 2010, the Applicants submitted the Huyghe Declaration, which provided a comparative experiment showing that the recited invention has superior properties over a hydrogel similar to the one disclosed in Malmonge.[57] These results rebut any *prima facie* showing of obviousness. *Ormco Corp. v. Align Technology, Inc.*, 463 F.3d 1299, 1311, 79 U.S.P.Q.2d 1931 (Fed. Cir. 2006); MPEP § 2145; see also *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995). Since these results were not expected, and since there is no evidence to suggest that they were expected, the Examiner's rejection should be reversed.

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[55] Huyghe Declaration at ¶ 7.

[56] Pissis at page 561, § 2.1.

[57] Huyghe Declaration at ¶ 8 and Exhibit B.

CONCLUSION

The Examiner has asserted two sets of rejections under 35 U.S.C. §103: one against claims 8, 9 and 12-15, and a second against claims 8, 10 and 11. Both sets of rejections are at least based on the combination of: Malmonge, Slivka, Pissis and Young. As discussed above, the Examiner has failed to provide the required motivation to combine these references, and the references teach away from the recited invention. Accordingly, claims 8-14 are patentable over these references. Reversal of all of the Examiner's rejections and allowance of claims 8-14 is respectfully requested.

Respectfully submitted,

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CLAIM APPENDIX

Claims 1-8 (Cancelled).

Claim 8: A material for cartilage-like material substitution, comprising a fibre-reinforced polymerized hydrogel, wherein said polymerized hydrogel contains 10-70% (m/m) swellable fibres (based on the dry matter), wherein the length of the fibres is at least a millimeter, and wherein 1-5% (m/m) (based on the dry matter) of a substance that contains ionized groups has been added to said polymerized hydrogel and, wherein said swellable fibres have sucked up at least one monomer solution prior to polymerization of the hydrogel.

Claim 9: The material for cartilage-like material substitution according to claim 8, wherein said monomer solution is a hydroxyethyl methacrylate (HEMA) polymer.

Claim 10: The material for cartilage-like material substitution according to claim 8, wherein said substance containing ionized groups comprises methacrylic acid.

Claim 11: The material for cartilage-like material substitution according to claim 10, comprising 1-5% (m/m) methacrylate.

Claim 12: The material for cartilage-like material substitution according to claim 8, wherein said swellable fibres comprise fibres saturated in a liquid.

Claim 13: The material for cartilage-like material substitution according to claim 8, wherein said swellable fibres comprise a polyurethane material.

Claim 14: A prosthesis fabricated of the material for cartilage-like material substitution of claim 8.

Claim 15: A material for cartilage-like material substitution, comprising a fibre-reinforced polymerized hydrogel, wherein said polymerized hydrogel contains 10-70% (m/m) swellable fibres (based on the dry matter), wherein the length of the fibres is at least a millimeter, and wherein 1-5% (m/m) (based on the dry matter) of a substance that contains ionized groups has been added to said polymerized hydrogel and, wherein said swellable fibres comprise at least one monomer solution.

EVIDENCE APPENDIX

1. **Declaration by Jacque Marie René Jan Huyghe dated May 15, 2009** (referred to as "Huyghe Declaration").

A copy of the Huyghe Declaration was filed with the United States Patent and Trademark Office on June 8, 2009 together with the Applicant's Amendment dated June 8, 2009. According to the Office Action dated August 18, 2009, this Declaration was considered by the Examiner (see page 9 of said Office Action).

RELATED PROCEEDING APPENDIX

There are no related proceedings.